EXHIBIT I – KETAMINE: CURRENT APPLICATIONS IN ANESTHESIA, PAIN AND CRITICAL CARE

Anesthesia Essays and Researches
Home
Current issue
Instructions
Submit article

Anesth Essays Res. 2014 Sep-Dec; 8(3): 283–290.
doi: 10.4103/0259-1162.143110
PMCID: PMC4258981
PMID: 25886322

Ketamine: Current applications in anesthesia, pain, and critical care

Madhuri S. Kurdi, Kaushic A. Theerth, and Radhika S. Deva

Department of Anaesthesiology, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India
Corresponding author: Dr. Madhuri S. Kurdi, Department of Anaesthesiology, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India. E-mail: drmadhuri_kurdi@yahoo.com

Abstract

Ketamine was introduced commercially in 1970 with the manufacturer's description as a “rapidly acting, nonbarbiturate general anesthetic” and a suggestion that it would be useful for short procedures. With the help of its old unique pharmacological properties and newly found beneficial clinical properties, ketamine has survived the strong winds of time, and it currently has a wide variety of clinical applications. It's newly found neuroprotective, antiinflammatory and antitumor effects, and the finding of the usefulness of low dose ketamine regimens have helped to widen the clinical application profile of ketamine. The present article attempts to review the current useful applications of ketamine in anesthesia, pain and critical care. It is based on scientific evidence gathered from textbooks, journals, and electronic databases.

Keywords: Anesthesia, clinical applications, critical care, drug, ketamine, pediatrics, pain, palliative care, perioperative analgesia

INTRODUCTION

Ketamine is in clinical use since 1970.[1] It is a unique intravenous (IV) anesthetic that produces a wide spectrum of pharmacological effects including sedation, catalepsy, somatic analgesia, bronchodilation, and sympathetic nervous system stimulation.[2] The availability of newer drugs, the disturbing emergence reactions of ketamine, its stigma as a “vet medicine” and gaining popularity as a drug with abuse potential are factors, which would discourage its use by present day anesthesiologists.[3,4] However, ketamine because of its unique properties and newly found clinical properties has stood

the test of time.[3,4,5,6,7] It has a wide range of clinical applications even today. Most of the modern anesthesiologists receive minimal training with ketamine.[8] They are not aware of the wide clinical applications of ketamine. Keeping this in mind, a thorough literature search was conducted through PubMed and Cochrane electronic databases. Various standard textbooks and journals of anesthesia were consulted. Based on this, the current indications of ketamine in anesthesia, pain and critical care are discussed in this review article.

PHARMACOLOGY OF KETAMINE IN BRIEF

Basic chemistry

Ketamine is a water soluble phencyclidine derivative. The ketamine molecule contains an asymmetric carbon atom with two enantiomers: The S(+) isomer and the R(−) isomer.[9]

Pharmacokinetics

Ketamine is highly lipid soluble and undergoes rapid breakdown and redistribution to peripheral tissues. It is metabolized extensively in the liver by N-demethylation and ring hydroxylation pathways.[1,10] Norketamine is the main metabolite and is one-third to one-fifth as potent as ketamine as an anesthetic. Ketamine is excreted in urine and faeces as norketamine and as hydroxylated derivatives. It has a cumulative effect. Gradual resistance builds up on repeated administration.[10]

Pharmacodynamics

Ketamine stimulates the cardiovascular system resulting in an increase in heart rate, blood pressure and increase in cardiac output, mediated principally through the sympathetic nervous system.[11] It has minimal effects on central respiratory drive and produces airway relaxation by acting on various receptors and inflammatory cascades and bronchial smooth muscles.[1,9] It increases salivation and muscle tone.[11] It has cataleptic, amnestic, profound analgesic, and dose dependent anesthetic actions.[10,11] The cataleptic state is an akinetic state with the loss of orthostatic reflexes, but without impairment of consciousness.[10,12] The dissociative state produced by ketamine is unique in which the patient appears awake, but is detached from the surroundings with eyes remaining open.[11]

Mechanism of action

Its mechanism of action is mainly by noncompetitive antagonism of the N-methyl D-aspartic acid (NMDA) receptor. It also interacts with opioid receptors, monoamine, cholinergic, purinergic and adrenoreceptor systems as well as having local anesthetic effects.[5]

Newly found mechanisms of action with newer clinical applications

1. NMDA receptor interaction with ketamine plays a role in the opioid induced antihyperalgesic effects of ketamine[5]
2. Subanesthetic doses of ketamine via NMDA receptor blockade potentiate opioid analgesia[7]
3. Ketamine by suppressing the induction of NO synthase activity and protein expression by endotoxin exerts a protective antiinflammatory effect against sepsis process[13]
4. The hypnotic effects of ketamine are caused by a combination of immediate channel blockade of NMDA and hyperpolarization-activated cation channels[6]
5. Its antiproinflammatory effects may be responsible for its antihyperalgesic effects[5]

6. Its immediate analgesic effects are mediated predominantly by a combination of opioid system sensitization and antinociception[6]

7. Ketamine inhibits tumor necrosis factor-alpha and interleukin-6 gene expressions in macrophages.[5] NMDA receptor blockade by ketamine inhibits extracellular signal regulated kinase ½ pathway and proliferation of carcinoma cells by cell cycle arrest[7]

8. Downstream "postdrug" effects such as activity induced increase in structural synaptic connectivity lead to the prolonged antidepressant effects of ketamine.[6]

CURRENT CLINICAL APPLICATIONS OF KETAMINE

Old well-established applications where the role of ketamine remains unchallenged

1. As an IV induction agent in the emergency setting in shocked or hypotensive patients: The combination of rapid blood - cerebral transfer kinetics, sympathomimetic hemodynamic effects and absence of idiosyncratic adverse effects like impaired steroidogenesis all confer distinct advantages on ketamine when used for rapid sequence induction in hemodynamically compromised patients.[14] A study showed that ketamine is a safe and valuable alternative to etomidate for endotracheal intubation in critically ill patients with sepsis.[15] Its free radical scavenging property, neuroprotective effects against cerebral ischemia, anticonvulsant activity, potential to limit hypotension and hypotension related secondary brain injury are favorable in patients with traumatic brain injury.[16] In patients with cardiac tamponade and restrictive pericarditis, ketamine provides excellent anesthetic induction, and maintenance.[1]

2. For patients with reactive airways disease:

    a. Ketamine by virtue of its bronchodilating property and profound analgesia allowing use of high oxygen concentration is considered to be the IV induction agent of choice in patients with active bronchospasm.[3] Some researchers have found that ketamine not only protected against precipitation of asthma in asymptomatic surgical patients, but it also alleviated bronchospasm in patients with respiratory distress prior to induction of anesthesia[9]

    b. Ketamine is considered to be the bronchodilator of choice in rescue therapy for refractory bronchospasm in OT and refractory status asthmaticus in the intensive care unit (ICU). A loading dose of 0.1–0.2 mg/kg followed by an infusion of 0.15–2.5 mg/kg/h can be used in these cases.[9]

3. For induction of patients especially children with congenital heart disease with right to left shunt: Ketamine is the anesthetic drug of choice in these cases due to its beneficial cardiovascular effects of increasing systemic vascular resistance and the resulting decrease in right to left shunt.[17] Furthermore, by increasing pulmonary blood flow, it improves oxygenation.[12] In a study, IV or intramuscular (IM) ketamine as induction agents did not significantly affect SaO_2% in patients with fallots tetralogy.[17] Ketamine appears as a good alternative to sevoflurane for induction in patients with congenital heart disease where it preserves intra- and post-operative hemodynamic stability.[18,19]

4. Burns: Ketamine has been widely used to provide analgesia in burn dressing changes, during excision and grafting and for sedation.[20] It has a major role in repeated anesthetics for burns dressings.[11] The major advantage of ketamine in burns is that unlike other agents, it usually preserves airway and spontaneous respiratory function in addition to providing good sedoanalgesia.[20] It is the most desirable agent for IM administration in patients with extensive burns where there a difficulty in finding a suitable vein.[10] A recent study has shown that

ketamine is generally effective and well-tolerated in pediatric burns patients.[21] Oral and IV ketamine have been used as an analgesic and sedative for wound care procedures in children with burns and provides improved analgesia and sedation.[20,22] Ketamine in combination with midazolam/dexmedetomidine provides effective sedoanalgesia without causing any significant side-effects.[20] Ketamine can be used in combination with propofol for burns dressings in adults and children.[23] A recent study showed that ketamine therapy given 15 min after burns injury in rats improves survival in severe burns injury probably by eliciting heat-shock response as evidenced by the expression of heat-shock protein 70 in myocardial cells and cerebral tissues.[24]

5. Prehospital and battlefield medicine: Ketamine is the anesthetic of choice when supplies of oxygen and monitoring and disposable equipment are limited.[25] The United States Defense Health Board notes that morphine is the slipping gold standard in Tactical Combat Casualty Care pain management and recommends ketamine as a new alternative to battlefield analgesia.[26] Ketamine is an effective agent in facilitating endotracheal intubation in the Helicopter Emergency Medical Services setting.[27] In military practice, ketamine is currently used throughout the entire military chain of evacuation from the point of wounding, through the field hospital and on to the receiving hospital in the United Kingdom. All doctors joining the army are given training in the use of ketamine for the treatment of pain.[4] Ketamine is added to opioids like morphine or transmucosal fentanyl to help the combat medic to control pain without the risk of opioid induced hypotension. Ketamine 50-100 mg IM or 50 mg intranasally using atomizer is given and repeated every 30 min to 1 h or until nystagmus appears.[26] Ketamine is an invaluable agent for treatment of the trapped casualty or even in the mass casualty situation.[11] It is used for sedation of the trapped casualty and also for pain control to facilitate extraction of the trapped casualty.[28]

6. In low doses (IV 0.5 mg/kg) in combination with IV diazepam or midazolam as an IV supplement to local and regional anesthesia techniques including spinal anesthesia in adults and children.[1] Low dose ketamine infusions (5–25 mg/kg/min) can be used for sedation and analgesia during local or regional anesthetic procedures.[1] They can be used before the application of painful blocks but are more commonly used for sedation or supplemental anesthesia during long uncomplicated procedures or supplemental analgesia for inadequate blocks in combination with IV diazepam.[1] IV ketamine 0.5 mg/kg given prophylactically just before neuraxial blockade decreases the incidence of shivering, improves hemodynamic profile, provides good sedation and prevents recall.[29] IV ketamine 1 mg/kg given before spinal anesthesia results in good hemodynamic stability in elderly patients undergoing transurethral resection of the prostate.[30]

Intermediate clinical applications currently in use with moderate scientific evidence and where ketamine is used as an option to other agents

1. In pediatrics:

    a. For premedication: This can be done by oral (3–10 mg/kg), intranasal, IM (2–4 mg/kg) or IV route in/not in combination with midazolam.[1] Because of its rapid onset of action, ketamine has been used as an IM induction drug in children and difficult to manage mentally retarded patients regardless of age[3]

    b. Ketamine alone or in combination with propofol provides attenuation of sevoflurane induced emergence agitation in pediatric patients.[31,32] It does this by providing good postoperative sedation and analgesia with good recovery criteria and hemodynamic stability[30]

c. As an adjunct to caudal blocks: Ketamine is found to increase the efficacy of pediatric caudal anesthesia when combined with local anesthesia in a dose of 0.5–1 mg/kg.[33] Caudal block under basal ketamine anesthesia is widely used for pediatric lower abdominal and lower limb surgeries in developing countries, especially for uncooperative children.[34] However, the safety of caudal/epidural ketamine has not received regulatory approval.[1]

2. As an adjunct to IV regional anesthesia (IVRA), peripheral nerve blocks, stellate ganglion blocks: Addition of ketamine 0.1 mg/kg to 0.5% lignocaine or ketamine 0.5 mg/kg to 1% lignocaine for IVRA increases tourniquet tolerance, improves the quality of anesthesia and decreases analgesic consumption.[35,36] Ketamine 0.5 mg/kg added as a local anesthetic adjunct for stellate ganglion block enhances the sympathetic blockade with longer pain relief.[37]

3. Prevention of postanesthesia shivering: Several prospective randomized controlled studies have shown that low dose prophylactic IV ketamine (0.25–0.75 mg/kg) is effective in preventing postanesthesia shivering.[38,39,40,41,42]

Recent clinical applications of ketamine with moderate scientific evidence and based on a renewed interest in low dose ketamine regimes

1. Procedural sedation for adults and children: The literature is strongly supportive of the safety and efficacy of ketamine for emergency department (ED) dissociative sedation for a variety of brief painful or emotionally disturbing procedures in both children and adults e.g.: Laceration repair, fracture reduction, abscess drainage, emergency cardioversion, amputation, chest tube insertion. It is useful for procedures in the mentally disabled who are often uncooperative.[43] This dissociative sedation can be readily achieved by administration of a single IV or IM loading dose of ketamine followed by titration.[43] Intranasal ketamine is being used in a wide range of clinical doses for procedural sedation in children (0.5-9 mg/kg).[44,45] It is used for sedation or general anesthesia for pediatric procedures like cardiac catheterization, radiation therapy, radiological studies such as magnetic resonance imaging, dressing changes, and dental work.[1,3,46] Ketamine in low doses in combination with low doses of propofol provides effective and safe sedo-analgesia in pediatric emergency short surgical procedures and in adults undergoing colonoscopy and short gynecological procedures[47,48,49]

2. Sedation and analgesia in the critical care unit: Ketamine used for patients in a critical care unit provides combined sedation and analgesia and has favorable effects on hemodynamics and can treat persistent bronchospasm.[1,2] Continuous IV infusion of ketofol provides adequate and safe short term sedation(<24 h) for critically ill patients in ICU.[50] Critical care physicians have nowadays warmed to the use of ketamine in limiting physiological disturbance during temporary distressing procedures like endotracheal suction for prolonged sedation even in known traumatic brain injury cases.[51] In septic patients with cardiovascular instability, ketamine because of its cardiovascular stimulatory effects reduces inotropic support and exerts a protective antiinflammatory effect against the sepsis process.[13] In a study in patients with intracranial hypertension undergoing mechanical ventilation, ketamine effectively decreased intracranial pressure (ICP) and prevented untoward ICP elevations during distressing interventions without lowering blood pressure and cerebral perfusion pressure. Thus, ketamine can be used in combination with a benzodiapine for patients with traumatic brain injury and intracranial hypertension and in trauma emergency situations[52]

3. Co-induction and total IV anesthesia (TIVA): As co-induction agent in low doses and in combination with other drugs like propofol/midazolam/dexmedetomidine for TIVA technique in the operating room, ketamine has gained increasing popularity. The advantages of this

combination are maintenance of stable hemodynamics, reduced pain of injection and minimal respiratory depression while allowing spontaneous ventilation.[1,53,54] In a study on 80 elderly patients, ketofol (ketamine and propofol 1:1 i.e. 5 mg/ml each) provided good proseal laryngeal mask airway insertion conditions and less requirement of ephedrine with more duration of apnea.[55]

Recent clinical applications with limited scientific evidence

These are based on a better understanding of the role of N-methyl D-aspartic acid receptors in pain modulation and on newly found antiinflammatory properties of ketamine.[3,4,5,6,7]

Acute pain management

1. For perioperative analgesia:
    a. IV low dose ketamine (0.5 mg/kg) is devoid of any hemodynamic changes and adverse effects and is an optimal dose for preemptive analgesia in laparoscopic cholecystectomy.[56,57] Preemptive intranasal ketamine 1.5 mg/kg enhances postoperative analgesia after endoscopic nasal surgery[58]
    b. Low dose regimes (in the range of IV 0.25–0.5 mg/kg as an initial bolus followed by 50–500 μg/kg/h) have been proposed as an adjunct for postoperative analgesia and for reduction of exogenous opioid induced hyperalgesia.[59,60] A recent review of randomized double blinded clinical trials of ketamine added to opioids in IV patient controlled analgesia for postoperative pain found that the ketamine-opioid combination significantly reduced pain scores, cumulative morphine consumption and postoperative desaturation in patients undergoing thoracic surgery[7]
    c. Low dose IV/subcutaneous (SC) ketamine 0.5 mg/kg at the end of surgery is safe and effective for posttonsillectomy pain control.[61] Ketamine spray (0.5 mg/kg) in tonsillar fossa is effective for posttonsillectomy pain control in children[62]
2. There are a limited number of reports that indicate the role of multimodal pain therapy including ketamine in preventing postoperative chronic pain.[1]
3. Low dose ketamine in the ED: Initial bolus of 0.2–0.3 mg/kg IV over 10 min with subsequent infusion of 0.1–0.3 mg/kg/h as an adjunct to commonly used opioids like morphine is recommended for ED pain management.[63]

Chronic pain management

a. Noncancer chronic pain: Ketamine has been used off-label, administered topically or intravenously in small, subanesthetic doses as an analgesic for treating chronic painful conditions.[64] The action of ketamine on opiate tolerance and hyperalgesia combined with its direct analgesic activity has prompted its increasing use in chronic pain states. On the basis of a few short term trials with limited clinical applications, ketamine may be effective in the treatment of chronic peripheral and central neuropathic pain, phantom and ischemic limb pain, fibromyalgia, chronic regional pain syndrome (CRPS), visceral pain and migraine.[1] Ketamine is usually used as an alternative therapy and for short terms in neuropathic pain management where the role of ketamine is very varied with the level of evidence II-IV.[65] IV ketamine given as an alternative drug infusion as 300 μg/kg in 60 ml solution over 3 h has been reported to give complete remission of phantom limb pain.[66] Low dose intranasal S(+) ketamine is beneficial for the *ad hoc* treatment of breakthrough pain in patients with neuropathic pain.[67]

Current literature suggests that ketamine can be used by various routes: IV, SC, and IM, epidural, intrathecal, intraarticular, intranasal, oral and topical for the short-term relief of refractory neuropathic pain. In these situations, rapid acting routes of administration like injection or intranasal route should be avoided and doses should be kept as low as possible.[68] A recommended starting dosage is 0.5 mg/kg racemic ketamine or 0.25 mg/kg of S-ketamine as a single oral dose. The dosage is increased by the same amount if required and given 3-4 times daily. Lack of evidence regarding efficacy and the poor safety profile do not support the routine use of oral ketamine in chronic pain management and it may have a limited place as an add-on therapy in complex chronic pain patients if other therapeutic options have failed.[69] Due to side-effects such as psychedelic symptoms, cardiovascular stimulation and hepatotoxicity, the use of ketamine should be restricted to patients with therapy resistant severe neuropathic pain.[70]

Two approaches to using ketamine to treat CRPS - one employing sub-anesthetic doses and the other employing anesthetic doses (ketamine coma) show promise according to researchers.[71] IV ketamine 7 mg/kg/h, dexmedetomidine 1.5 μg/kg/h and midazolam 17 mg/h has been used to induce medical coma for 5 days in patients with CRPS to get good results.[72] A randomized controlled trial (RCT) in 21 patients with refractory CRPS showed that ketamine infusion over 4 h for 5 days at a maximum of 0.35 mg/kg/h produced 21.4% reduction in pain compared with placebo.[73]

b. Cancer pain: In palliative care practice, ketamine has been administered as a co-analgesic in addition to opioids and co-adjuvant drugs. Ketamine is now considered to be an essential adjuvant analgesic for refractory cancer pain, and it is on the WHO's essential drugs list for patients who no longer respond to high doses of opioids or have predictable breakthrough pains.[74] Ketamine is generally administered orally, by IV injection, SC injection, continuous SC infusion, IM injection, sublingually, intranasally and per rectum.[75] For analgesia, initial oral doses are 2-25 mg three to four times a day, increased to 40–60 mg 4 times a day. IV doses for analgesia are 2.5–5 mg as required and 0.5–1 mg/kg to cover procedures associated with pain. SC doses are typically 2.5–25 mg with continuous SC injection given at a dose of 50–100 mg/24 h increased gradually if required to 600 mg/24 h.[4,76] Preliminary evidence of case reports suggests that oral ketamine may produce fewer adverse effects and also that oral ketamine may be more potent than SC ketamine.[77] A constant intrathecal dose of S-ketamine, at 22.5 mg/day in combination with morphine for 3 months has been reported to produce good pain relief in a patient with leg pain due to urethral carcinoma and metastasis.[77] NMDA receptor antagonism with ketamine has been found to exert antitumor effects.[7] A 2012 Cochrane review of the use of ketamine in cancer pain found 2 RCTs suggesting that ketamine as an adjunct to morphine improves the effectiveness of morphine in cancer pain. Among 32 case reports in the same review, the majority (28/32) described improved pain control with ketamine. Adverse effects commonly reported were sedation and hallucinations and they were not severe.[78]

MISCELLANEOUS CLINICAL APPLICATIONS OF KETAMINE BASED ON FEW CASE REPORTS

1. Cardiopulmonary bypass (CPB) surgery: Some authors have reported that a single dose of ketamine 0.5 mg/kg given upon induction was associated with lower serum levels of C-reactive protein and lower incidence of delirium and cognitive dysfunction after cardiac surgery with CPB. This is because of the neuroprotective and antiinflammatory effects of ketamine[79]
2. Use of dexmedetomidine and ketamine infusions during scoliosis repair surgery with somatosensory and motor evoked potential monitoring has been reported in a 15-year-old girl[80]

3. Ketamine sedation during spinal anesthesia for arthroscopic knee surgery can reduce the ischemic-reperfusion injury.[81] Ketamine by inhibition of NMDA receptor activation can attenuate opioid-induced degeneration of spinal motor neurons[7]
4. In electroconvulsive therapy (ECT): A study showed that S-ketamine given for ECT decreased the number of ECT sessions, produced lower depression severity scores and higher cognitive ratings.[82] In another study, ketamine appeared to be associated with a better word recall than etomidate after a course of 6 ECTs.[83] A study showed that ketamine-propofol combination (ketofol) can be an alternative strategy to enhance the seizure quality and clinical efficiency of ECT[84,85,86]
5. Ketamine gargle attenuates postoperative sore throat[87,88]
6. By virtue of NMDA antagonism, ketamine in small doses improves the postoperative depressive state in patients with mental depression[3]
7. A case report describes symptomatic improvement possibly by inhibition of neuroinflammation in the spinal cord in two patients with restless leg syndrome treated with oral ketamine[3]
8. Intrathecal administration of ketamine (5-50 mg in 3 ml of saline) produces brief and variable analgesia. However, its systemic effects occur after systemic absorption[3]
9. It has been used in patients with liver damage, acute intermittent porphyria and in hiccoughs[10]
10. Ketamine co-administered with fentanyl and propofol anesthesia for orthopedic surgery appears to have potent rapid antidepressant like properties thus improving the postoperative state of depressed patients.[89]

Though ketamine has many clinical applications, there are some limitations in its use about which one must be aware.

LIMITATIONS AND WARNINGS FOR KETAMINE USE

1. The increase in muscle tone produced by ketamine makes it unsuitable for operations where muscle relaxation is needed[11]
2. It is not indicated in conditions like hypertension, schizophrenia and raised intraocular pressure[10]
3. Though ketamine well maintains the airway, some form of airway compromise needing manipulation can occur[11]
4. The increase in salivation produced by ketamine can be troublesome and may produce laryngospasm in children.[10,12] Premedication with an antisialogogue may be needed[10]
5. It produces dose dependent psychological manifestations like emergence reactions, dreams, hallucinations and long-term psychotomimetic effects[10]
6. Ketamine is popularly known as a “vet medicine” and many people consider this as a stigma[3,4]
7. Ketamine has the potential to cause addiction[68]
8. Ulcerative cystitis, secondary renal damage and hepatic failure can occur with high doses of oral ketamine[68]
9. Frequent ketamine abuse can cause long standing memory impairment[62]

10. Anesthetic concentrations of ketamine could exert antagonistic actions on both μ and k opioid receptors and hence high doses of ketamine may not be an appropriate addition to opioids[7]

11. Epidural and spinal routes of administration of ketamine are generally not recommended due to unclear toxicity issues[68]

12. High dose ketamine accentuates apoptosis in the newborn brain of animals.[1] Release of neurotoxic mediators may cause neuronal apoptosis and consequent neuronal damage in humans.[68]

CURRENT WORLD STATUS OF THE CLINICAL APPLICATIONS OF KETAMINE

In developing nations

Millions of older adults in the developing world have safely received ketamine in the past 40 years where the drug continues to be widely administered in the operation theatres as an inexpensive and simple alternative to inhalational anesthesia.[43] In African countries and rural India where there is a paucity of anesthetic manpower, equipment and money, ketamine plays a major role in anesthetic service delivery in secondary health care facilities and in high-risk cases in tertiary institutions. It is always available in most of the hospitals and all anesthetists are familiar with it. It is widely used for elective and emergency procedures in children and adults.[90] Difficult airway cases are many a times managed with ketamine and facemask ventilation as availability of difficult airway gadgets is considered a luxury.[91]

In developed countries

The use of ketamine is reserved in specific cases such as hemorrhagic shock, hemodynamic instability, and bronchodilation. Its use is being expanded in the field of analgesia: Preemptive analgesia, as an adjunct to opioids for postoperative pain management, in chronic pain states and in the ED in sedation of children.[90] In civilian practice in the United Kingdom, ketamine is most commonly used as an anesthetic in the prehospital setting. It is particularly used for pediatric sedation in painful or frightening procedures. Less commonly, it is used in adult patients in the ED for dissociative sedation, and it is also used as an analgesic e.g.: In major trauma.[4]

CONCLUSION

Ketamine by virtue of some of its unique pharmacological advantages and newly found clinical properties has a wide range of clinical applications. The use of ketamine is extending now beyond the field of anesthesia into pain, palliative care, intensive care, and procedural sedation. It is being used more in low doses and as an adjunct to other drugs.

Footnotes

Source of Support: Nil

Conflict of Interest: None declared.

REFERENCES

1. Reves JG, Glass PS, Lubarsky DA, McEvoy MD, Ruiz RM. Intravenous anaesthetics. In: Miller RD, editor. *Miller's Anaesthesia.* 7th ed. USA: Churchill Livingstone; 2010. pp. 719–71. [Google Scholar]

2. White PF, Elig MR. Intravenous anaesthetics. In: Barash PG, editor. *Clinical Anaesthesia.* 6th ed. China: Lippincott Williams and Wilkins; 2013. pp. 478–500. [Google Scholar]